

CLAIMS

What is claimed is:

1. A method of stimulating cartilage growth or repair at a site in a subject in need of such growth or repair, said method comprising the step of administering to the site a therapeutically effective amount of an agonist of the non-proteolytically activated thrombin receptor.
2. The method of Claim 1 wherein the site is an arthritic joint.
3. The method of Claim 1 wherein the site is being treated for cartilage damage or loss.
- 10 4. The method of Claim 1 wherein the site is being treated for cartilage damage or loss due to traumatic injury.
5. The method of Claim 1 wherein the agonist is a thrombin peptide derivative comprising a polypeptide represented by the following structural formula:

15 Asp-Ala-R;

wherein R is a serine esterase conserved sequence.
6. The method of Claim 5 wherein the thrombin peptide derivative has between about 12 and about 23 amino acids.
7. The method of Claim 6 wherein the serine esterase conserved sequence has the amino acid sequence of SEQ ID NO. 1 (Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val), or a C-terminal truncated fragment thereof having at least six amino acids, provided that zero, one, two or three amino acids in the serine esterase conserved sequence differ from the corresponding position of SEQ ID NO 1.

8. The method of Claim 6 wherein the serine esterase conserved sequence has the amino acid sequence of SEQ ID NO. 1 (Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val), or a *C*-terminal truncated fragment thereof having at least nine amino acids, provided that zero, one or two of the amino acids in the serine esterase conserved region are conservative substitutions of the corresponding amino acid in SEQ ID NO 1.

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9. The method of Claim 6 wherein the serine esterase conserved sequence has the amino acid sequence of SEQ ID NO 2 (Cys-X₁-Gly-Asp-Ser-Gly-Gly-Pro-X₂-Val, wherein X₁ is Glu or Gln and X₂ is Phe, Met, Leu, His or Val), or a *C*-terminus truncated fragment of SEQ ID NO 2, said fragment having at least six amino acids.

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10. The method of Claim 9 wherein the thrombin peptide derivative comprises the amino acid sequence Arg-Gly-Asp-Ala (SEQ ID NO 3).

11. The method of Claim 10 wherein the thrombin peptide derivative comprises the amino acid sequence Arg-Gly-Asp-Ala-Cys-X₁-Gly-Asp-Ser-Gly-Gly-Pro-X₂-Val (SEQ ID NO 4), wherein X₁ is Glu or Gln and X₂ is Phe, Met, Leu, His or Val.

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12. The method of Claim 11 wherein the thrombin peptide derivative has the amino acid sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val- (SEQ ID NO 5), or an *N*-terminal truncated fragment thereof, provided that zero, one, two or three amino acids at positions 1-9 in the thrombin peptide derivative differ from the amino acid at the corresponding position of SEQ ID NO 5.

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13. The method of Claim 11 wherein the thrombin peptide derivative has the amino acid sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-

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Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val- (SEQ ID NO 5), or an *N*-terminal truncated fragment thereof, provided that zero, one or two amino acids at positions 1-9 in the thrombin peptide derivative are conservative substitutions of the amino acid at the corresponding position of SEQ ID NO 5.

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14. The method of Claim 12 wherein the thrombin peptide derivative is administered in a pharmaceutical composition additionally comprising an implantable, biocompatible carrier.
15. The method of Claim 14 wherein the carrier comprises a polylactic acid/polyglycolic acid homopolymer or copolymer .
16. A method of stimulating cartilage growth or repair at a site in a subject in need there such growth or repair, said method comprising the step of administering to the site a therapeutically effective amount of a peptide having the sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val (SEQ ID NO 5).
17. A method of stimulating cartilage growth at an arthritic joint in a subject, said method comprising the step of administering to the site a therapeutically effective amount of a peptide having the sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val (SEQ ID NO 5).
18. A method of stimulating cartilage growth in a subject at a site being treated for cartilage loss, said method comprising the step of administering to the site a therapeutically effective amount of a peptide having the sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val (SEQ ID NO 5).

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19. A method of stimulating cartilage growth in a subject at a site being treated for cartilage loss due to traumatic injury, said method comprising the step of administering to the site a therapeutically effective amount of a peptide having the sequence Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-
5 Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val (SEQ ID NO 5).

20. A method for culturing chondrocytes *in vitro*, the improvement comprising culturing the chondrocytes in the presence of a stimulating amount of an NPAR agonist.

10 21. The method of Claim 20, further comprising the step of administering a therapeutically effective amount of the cultured chondrocytes to a site in a subject in need of cartilage repair or growth.